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Hiccups With Dose Titration of Aripiprazole

To the Editor: Hiccups are characterized by repeated, involuntary spasmodic contractions of the diaphragm and inspiratory muscles followed by sudden closure of the glottis. Hiccups may be caused by infections, gastric distension, gastroesophageal reflux, or irritation of the phrenic or vagus nerves.¹

Aripiprazole is an atypical antipsychotic used in the treatment of a number of psychiatric conditions. Aripiprazole is a partial dopamine agonist-antagonist, unlike other antipsychotics that are primarily dopamine antagonists.

To our knowledge, there is only 1 case report² of an adolescent patient whose hiccups appeared with aripiprazole dose titration. Described here is a case of an adult patient who developed hiccups with aripiprazole during dose titration.

Case report. A 53-year-old white woman with a long history of depression and anxiety who was treated with multiple antidepressants in the past was started on aripiprazole as an adjunctive therapy to duloxetine. She was initially started on a daily dose of aripiprazole 5 mg, which she tolerated well and resulted in some improvement of her symptoms of depression. After 4 months of treatment, the dose was increased to 10 mg/d in an effort to achieve further improvement. A week after increasing the dose, she reported acute, persistent hiccups, occurring 12–15 times per day. The frequency and intensity of the hiccups impacted her everyday life, including her sleep, which was often interrupted. The dose of aripiprazole was reduced to 5 mg, which led to a decrease in her hiccups within 3 days to 2 to 3 times per day. After 2 months at the lower dose, aripiprazole was discontinued with complete disappearance of her hiccups.

Hypo- and hyperdopaminergic states and serotonergic medications are implicated in the pathophysiology of hiccups.³ Dopamine antagonists are often recommended to treat hiccups. However, the partial dopamine agonist actions of aripiprazole may contribute to the etiology of hiccups. While there are cases in which

aripiprazole-induced hiccups have been reported in association with brain injuries⁴ and hyponatremia⁵ and also in a patient with no predisposing factors,² this is the only case reported in an adult in whom the development and frequency and intensity of hiccups were dose related. Clinicians should be aware that hiccups can develop with dose increases of aripiprazole and decreasing the dose could be an effective treatment.

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